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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/598,048

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Robert R. Rando

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EXAMINER

SZNAIDMAN, MARCOS L

ART UNIT

PAPER NUMBER

1612

MAIL DATE

DELIVERY MODE

03/01/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/598,048	Applicant(s) RANDO, ROBERT R.	
	Examiner MARCOS SZNAIDMAN	Art Unit 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 January 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 271-276 is/are pending in the application.
- 4a) Of the above claim(s) 274 and 275 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 271-273 and 276 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1 page / 01/15/10</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to applicant's reply filed on January 15, 2010.

Status of Claims

Amendment of claim 271 is acknowledged.

Claims 271-276 are currently pending and are the subject of this office action.

Claims 274-275 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 17, 2009.

Claims 271-273 and 276 are presently under examination.

Priority

The present application is a 371 of PCT/US05/004990 filed on 02/17/2005, and claims priority to provisional application No. 60/578,324 filed on 06/09/2004, No. 60/567,604 filed on 05/03/04 and 60/545,456 filed on 02/17/04.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional

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application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Applications No. 60/545,456 and 60/567,604, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Application 60/545,456 and 60/567,604 fail to disclose the use of fenretinide. Accordingly, none of the examined claims (271-273 and 276) are entitled to the benefit of the prior applications. The priority date for all the claims is 06/09/2004 corresponding to provisional application No. 60/578,324.

Claim Rejections - 35 USC § 103 (New Rejection Necessitated by Amendment).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

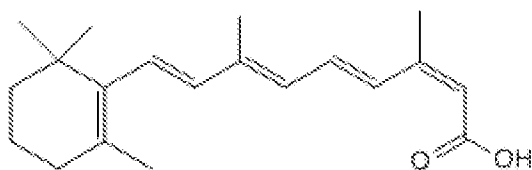
Claims 271-273 and 276 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf (Nutrition Reviews (2003) 61:342-346) in view of Campochiaro et. al. (US 6,075,032, cited in prior office action) and in view of Fanjul et. al. (The Journal of Biological Chemistry (1996) 271:22441-22446, cited in prior office action).

Claims 271-273 and 276 recite a method of treating an ophthalmologic disorder characterized by an accumulation of retinotoxic compounds in the cells of the retinal pigment epithelium (macular degeneration in claim 273) in a subject comprising

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administering to the subject a pharmaceutically acceptable amount of fenretinide or a pharmaceutically acceptable salt thereof.

For claims 271-273 and 276 Wolf teaches (see abstract) a method for treating macular degeneration by preventing the accumulation of A2E (a retinotoxic compound) by administering the drug isotretinoin (13-cis-retinoic acid or 13-cis RA) which has the following structure:



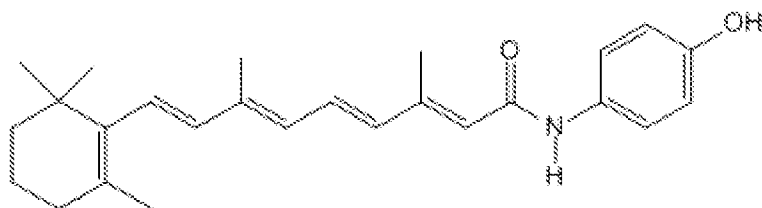
The authors further teach that administration of isotretinoin to old wild-type mice for 2 months reduced the amount of A2E by 40% when compared with untreated mice (see page 345, right column, first paragraph and figure 6). Finally the authors mention that “the danger of side effects in humans, such as birth defects in pregnant women and depression and suicide reported in many cases of isotretinoin treatment, would preclude long-term therapy with this drug” (see page 345, right column, last paragraph).

Wolf does not teach a method of treating macular degeneration associated with the accumulation of retinotoxic compounds like A2E with fenretinide.

However Campochiaro teaches that isotretinoin is a Retinoic Acid Receptor (RAR) agonist which is also a potent antagonist of AP1-dependent gene expression (see abstract, column 12, lines 65-67 and column 16, Table 3, second compound from the

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top). Fanjul teaches that fenretinide (4-hydroxyphenyl retinamide or 4HPR), which has the following structure:



is also a selective RAR agonist with anti AP-1 activity (see for example Abstract, also under Results on page 22442, also page 22443 under *4HPR Transrepression selectivity is distinct from its transactivation*, and on page 22445 under discussion, second paragraph). Fanjul further teaches that fenretinide has low toxicity (see abstract).

In summary, the prior art (Campochiaro and Fanjul) teach that isotretinoin and fenretinide belong to the family of compounds known as retinoids and that both are RAR agonists and antagonists of AP1-dependent gene expression.

Since Wolf teaches of treating macular degeneration associated with the accumulation of retinotoxic compounds like A2E with isotretinoin, and since Campochiaro and Fanjul teach that isotretinoin and fenretinide are structurally similar compounds that belong to the family of retinoids that are RAR agonists and antagonize AP-1, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any retinoid which is a RAR agonist that also antagonizes AP-1, like isotretinoin) for another (fenretinide) with an expectation of success, since the prior art establishes that both function in similar manner. The skilled

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in the art will be further motivated to replace isotreonin with fenretinide, since the prior art teaches that isotreonin is toxic for humans while fenretinide has shown very low toxicity.

Although the prior art is silent regarding the statements in claims 272: “wherein fenretinide inhibits, antagonizes, or short circuits the visual cycle at a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell” and claim 276: “wherein fenretinide increases the rate at which 11-cis-retinal is isomerized to all-trans-retinal; inhibits, antagonizes, or short circuits the visual cycle in the retinal pigment epithelium; inhibits at least one of lecithin retinol acyl transferase, isomerohydrolase, and 11-cis-retinol dehydrogenase, or inhibits binding to RPE65”, these limitations naturally flow from the method made obvious by Wolf in view of Campochiaro and Fanjul (see above), since the same compound: fenretinide, is being used to treat the same disease: macular degeneration. In other words, products of identical or similar composition cannot exert mutually exclusive properties when administered under the same circumstances. MPEP 2112 I states: “The discovery of a previously unappreciated property of a prior art composition or a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer”. *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999).

Apparently Applicant has discovered a new mechanism of action (“fenretinide inhibits, antagonizes, or short circuits the visual cycle at a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell” or “fenretinide increases the rate at which 11-cis-retinal is isomerized to all-trans-retinal; inhibits, antagonizes, or short

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circuits the visual cycle in the retinal pigment epithelium; inhibits at least one of lecithin retinol acyl transferase, isomerohydrolase, and 11-cis-retinol dehydrogenase, or inhibits binding to RPE65”) of an obvious invention (treating macular degeneration with fenretinide). The explanation of an effect or mechanism of action obtained when using a compound (e.g. increasing the rate at which 11-cis-retinal is isomerized to all-trans-retina) cannot confer novelty on a known or obvious process (administering fenretinide to patients with macular degeneration) if the skilled artisan was already aware of the occurrence of the desired therapeutic effect. Though new properties of a compound or their mechanism of action are no doubt important contributions to scientific and pharmaceutical development, the assessment of patentability is based upon the therapeutic applications and effects of the compounds, not the mechanism or properties by which they exert such a therapeutic effect.

Mere recognition of latent properties in the prior art does not render non-obvious an otherwise known invention. *In re Wiseman*, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. *In re Baxter Travenol Labs*, 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP 2145.

All this would result in the practice of claims 271-273 and 276 with a reasonable expectation of success.

Withdrawn Rejections and/or Objections

Claims rejected under 35 USC 112, first paragraph (scope of enablement).

Due to applicant's amendment of claim 271, the scope of enablement rejection is now moot.

Rejection under 35 USC 112, first paragraph (scope of enablement) is withdrawn.

Claims rejected under 35 USC 103(a)

Due to applicant's amendment of claim 271, the 35 USC 103(a) rejection is now moot.

Rejection under 35 USC 103(a) is withdrawn.

However, based on new prior art, a new 35 USC 103(a) rejection (necessitated by amendment) was applied (see above).

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
February 8, 2010.

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612